REMARKS

I. STATUS OF THE CLAIMS

Claims 1-3, 6-14 and 18-25 are pending. Claims 4, 5, 15, 16, 17, and 26-62 were previously canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications to any canceled subject matter.

Claim 1 is amended for grammatical clarity so that the method reads "measuring a first [or second] PAK4 phosphorylation level on ser-474" instead of "measuring a first [or second] PAK4 on ser-474 phosphorylation level."

Claim 6 is amended to recite various cancers that are literally disclosed in the fifth paragraph under the Detailed Description at page 11 of Applicants' priority document, USSN 60/429,363.

Since none of these amendments introduce new matter, Applicants respectfully request their entry into the record.

Applicants thank Examiner Aeder for his detailed comments in the Advisory Action dated May 12, 2008.

II. REJECTION UNDER 35 U.S.C. § 112

The rejection of claims 1-3, 6-14, and 18-25 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement, is maintained. Office Action dated 01/09/08 at page 3. The Office states that "the specification provides no working examples of the claimed invention" and that "there has been no demonstration showing that administered compositions that reduce PAK4 phosphorylation on ser-474 result in every or any therapeutic effect." *Id.* at page 3.

Applicants respectfully disagree that the originally-filed specification lacks sufficient guidance and methodological details to satisfy Section 112, first paragraph's enablement requirement. To further corroborate the enabling nature of their specification, however, Applicants provide data appended to the "Piraino Declaration" submitted herewith which evidences the ability of certain compositions to reduce PAK4/ser-474 phosphorylation in the sampled cancers. Hence, the Declarant, an employee of the assignee, relates the corroborative results of PAK4/ser-474 phosphorylation studies that he had performed in 2005-2006 and the usefulness of therapeutic compositions to monitor the effect of

phosphorylation state before and after administration of the composition. Please see paragraph 5 of the Declaration.

To elaborate, the Declarant took non-small cell lung cancer samples, colon cancer samples, and skin samples from animals and measured PAK4/ser-474 phosphorylation levels before and after exposure to certain compositions. Please see paragraphs 6-7 (NSCLC) and 8-10 (colon cancer). In paragraph 11, the Declarant explains that he followed the immunohistochemical staining protocol set forth in Applicants' specification (paragraph [0052] of the published version of the application, US 2005/0054017); and that he incubated the samples with the primary antibody disclosed in the application.

Exhibit B (paragraph 7) depicts the results of the lung cancer test and showed that PAK4 ser-474 phosphorylation "is lower when [the inhibitory composition] had been administered to the animal as compared to the control." Similarly, Exhibit C (paragraphs 9 and 10) depicts graphical data showing "decrease in the basal level of phosphorylation of PAK4 at activation residue ser474 in both the [colon] tumor section and the skin section."

The Declarant therefore concludes that "these experiments demonstrate that therapeutic compositions . . . reduce PAK4 phosphorylation on serine-474 in tumorgenic samples" and that "[F]urthermore, reduction in PAK4 corresponds to anti-tumor activity in preclinical mouse xenograft models." Please see paragraph 12.

The Piraino Declaration fully corroborates that at the time of filing Applicants' specification related detailed guidance and provided a level of expectation with respect to the applicability of the disclosed methods across different cancers. The skilled person, after reading Applicants' specification, would have (1) known cancer cells overexpress phosphorylated PAK4 on ser-474; (2) learned what methods and antibody tools can be used to determine PAK4/ser-474 phosphorylation levels; and (3) been able to screen candidate compositions to determine whether any one of them reduces PAK4/ser-474 phosphorylation levels, so that the detrimental consequences of cancer, such as anchorage-independent growth, can be inhibited or slowed by shutting down PAK4/ser-474 phosphorylation. The data and evidence provided in Mr. Piraino's declaration corroborates this enabling disclosure. Applicants therefore respectfully assert that the claimed invention is enabled for all of the foregoing reasons and respectfully request withdrawal of this rejection.

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Applicants invite Examiner Aeder to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.